

SEQUENCE LISTING



<110> Pecker, Iris

Vlodavsky , Israel

Feinstein, Elena

<120> POLYNUCLEOTIDE ENCODING A POLYPEPTIDE HAVING HEPARANASE ACTIVITY AND EXPRESSION OF SAME IN GENETICALLY MODIFIED CELLS

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<170> PatentIn version 3.1

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Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly  
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Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu  
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| cga gta tac ctt cat tgc aca aac act gac aat cca agg tat aaa gaa<br>Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu<br>435 440 445     | 1403 |
| gga gat tta act ctg tat gcc ata aac ctc cat aac gtc acc aag tac<br>Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr<br>450 455 460     | 1451 |
| ttg cgg tta ccc tat cct ttt tct aac aag caa gtg gat aaa tac ctt<br>Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu<br>465 470 475     | 1499 |
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Leu Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg  
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Pro Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala  
100 105 110

Asn Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys  
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Leu Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly  
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Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu

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|     |     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     |

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| ttc ctc atc ctc ctg ggt tct cca aag ctt cgt acc ttg gcc aga ggc<br>Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu Arg Thr Leu Ala Arg Gly<br>120 125 130 135 | 498  |
| ttg tct cct gcg tac ctg agg ttt ggt ggc acc aag aca gac ttc cta<br>Leu Ser Pro Ala Tyr Leu Arg Phe Gly Thr Lys Thr Asp Phe Leu<br>140 145 150         | 546  |
| att ttc gat ccc aag aag gaa tca acc ttt gaa gag aga agt tac tgg<br>Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe Glu Glu Arg Ser Tyr Trp<br>155 160 165     | 594  |
| caa tct caa gtc aac cag gat att tgc aaa tat gga tcc atc cct cct<br>Gln Ser Gln Val Asn Gln Asp Ile Cys Lys Tyr Gly Ser Ile Pro Pro<br>170 175 180     | 642  |
| gat gtg gag gag aag tta cgg ttg gaa tgg ccc tac cag gag caa ttg<br>Asp Val Glu Glu Lys Leu Arg Leu Glu Trp Pro Tyr Gln Glu Gln Leu<br>185 190 195     | 690  |
| cta ctc cga gaa cac tac cag aaa aag ttc aag aac agc acc tac tca<br>Leu Leu Arg Glu His Tyr Gln Lys Lys Phe Lys Asn Ser Thr Tyr Ser<br>200 205 210 215 | 738  |
| aga agc tct gta gat gtg cta tac act ttt gca aac tgc tca gga ctg<br>Arg Ser Ser Val Asp Val Leu Tyr Thr Phe Ala Asn Cys Ser Gly Leu<br>220 225 230     | 786  |
| gac ttg atc ttt ggc cta aat gcg tta tta aga aca gca gat ttg cag<br>Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Ala Asp Leu Gln<br>235 240 245     | 834  |
| tggt aac agt tct aat gct cag ttg ctc ctg gac tac tgc tct tcc aag<br>Trp Asn Ser Ser Asn Ala Gln Leu Leu Asp Tyr Cys Ser Ser Lys<br>250 255 260        | 882  |
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| att caa ttg cat aaa ctt cta aga aag tcc acc ttc aaa aat gca aaa<br>Ile Gln Leu His Lys Leu Leu Arg Lys Ser Thr Phe Lys Asn Ala Lys<br>300 305 310     | 1026 |
| ctc tat ggt cct gat gtt ggt cag cct cga aga aag acg gct aag atg<br>Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg Arg Lys Thr Ala Lys Met<br>315 320 325     | 1074 |
| ctg aag agc ttc ctg aag gct ggt gga gaa gtg att gat tca gtt aca<br>Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Val Thr<br>330 335 340     | 1122 |
| tggt cat cac tac tat ttg aat gga cgg act gct acc agg gaa gat ttt<br>Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg Glu Asp Phe<br>345 350 355    | 1170 |
| cta aac cct gat gta ttg gac att ttt att tca tct gtg caa aaa gtt<br>Leu Asn Pro Asp Val Leu Asp Ile Phe Ile Ser Ser Val Gln Lys Val<br>360 365 370 375 | 1218 |
| ttc cag gtg gtt gag agc acc agg cct ggc aag aag gtc ttg tta gga<br>Phe Gln Val Val Glu Ser Thr Arg Pro Gly Lys Lys Val Trp Leu Gly<br>380 385 390     | 1266 |
| gaa aca agc tct gca tat gga ggc gga gcg ccc ttg cta tcc gac acc<br>Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asp Thr<br>395 400 405     | 1314 |
| ttt gca gct ggc ttt atg tgg ctg gat aaa ttg ggc ctg tca gcc cga<br>Phe Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Arg<br>410 415 420     | 1362 |
| atg gga ata gaa gtg gtg atg agg caa gta ttc ttt gga gca gga aac<br>Met Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn                    | 1410 |

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| aac act gac aat cca agg tat aaa gaa gga gat tta act ctg tat gcc<br>Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly Asp Leu Thr Leu Tyr Ala<br>490 495 500     |     |     | 1602 |
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&lt;210&gt; 44

&lt;211&gt; 535

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 44

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Ala Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp  
20 25 30

Leu Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe  
35 40 45

Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu  
50 55 60

Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser  
65 70 75 80

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe  
85 90 95

Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser  
100 105 110

Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val  
115 120 125

Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu  
130 135 140

Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser  
145 150 155 160

Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu  
165 170 175

Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn  
180 185 190

Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr  
195 200 205

Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys  
210 215 220

Ala His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu  
225 230 235 240

Leu His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr  
245 250 255

Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg  
260 265 270

Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His  
 275 280 285

His Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser  
 290 295 300

Ser Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys  
 305 310 315 320

Val Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr  
 325 330 335

Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala  
 340 345 350

Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly  
 355 360 365

Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His  
 370 375 380

Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu  
 385 390 395 400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys  
 405 410 415

Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val  
 420 425 430

Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn  
 435 440 445

Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg  
 450 455 460

Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu  
 465 470 475 480

Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp  
 485 490 495

Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser  
 500 505 510

Ala Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn  
 515 520 525

Ala Lys Ile Ala Ala Cys Ile  
 530 535

<210> 45

<211> 2396

<212> DNA

<213> Mus musculus

<220>



&lt;221&gt; CDS

&lt;222&gt; (594)..(2198)

&lt;223&gt;

&lt;400&gt; 45

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ttaaggcaga agggagtcgg ggtagggctc ggctgaaccc tcaaccgggg cttttaactc      180
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accaggaagc tgggtcccacc cctgcgcggc tcccggggcg tccctcccca ggcctccgag      300
gatcttggat tctggccacc tccgcaccct ttggatgggt gtggatgatt tcaaaagtgg      360
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cagcgcgccg gctgcccag ctctcccggc agcgggcggt ccagccaggt ggg atg      596
                                   Met
                                   1
ctg agg ctg ctg ctg ctg tgg ctc tgg ggg ccg ctc ggt gcc ctg gcc      644
Leu Arg Leu Leu Leu Leu Trp Leu Trp Gly Pro Leu Gly Ala Leu Ala
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cag ggc gcc ccc gcg ggg acc gcg ccg acc gac gac gtg gta gac ttg      692
Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp Leu
                                   20                                25                                30
gag ttt tac acc aag cgg ccg ctc cga agc gtg agt ccc tcg ttc ctg      740
Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe Leu
                                   35                                40                                45
tcc atc acc atc gac gcc agc ctg gcc acc gac ccg cgc ttc ctc acc      788
Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu Thr
                                   50                                55                                60                                65
ttc ctg ggc tct cca agg ctc cgt gct ctg gct aga ggc tta tct cct      836
Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser Pro
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gca tac ttg aga ttt ggc ggc aca aag act gac ttc ctt att ttt gat      884
Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp
                                   85                                90                                95
ccg gac aag gaa ccg act tcc gaa gaa aga agt tac tgg aaa tct caa      932
Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser Gln
                                   100                                105                                110
gtc aac cat gat att tgc agg tct gag ccg gtc tct gct gcg gtg ttg      980
Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val Leu
                                   115                                120                                125
agg aaa ctc cag gtg gaa tgg ccc ttc cag gag ctg ttg ctg ctc cga      1028
Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu Arg
                                   130                                135                                140                                145
gag cag tac caa aag gag ttc aag aac agc acc tac tca aga agc tca      1076
Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser
                                   150                                155                                160
gtg gac atg ctc tac agt ttt gcc aag tgc tcg ggg tta gac ctg atc      1124
Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu Ile
                                   165                                170                                175
ttt ggt cta aat gcg tta cta cga acc cca gac tta cgg tgg aac agc      1172
Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn Ser
                                   180                                185                                190
tcc aac gcc cag ctt ctc ctt gac tac tgc tct tcc aag ggt tat aac      1220
Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn
                                   195                                200                                205

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| cac att ctc atc gat ggg ttg cag tta gga gaa gac ttt gtg gag ttg<br>His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu Leu<br>230 235 240     | 1316 |
| cat aaa ctt cta caa agg tca gct ttc caa aat gca aaa ctc tat ggt<br>His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr Gly<br>245 250 255     | 1364 |
| cct gac atc ggt cag cct cga ggg aag aca gtt aaa ctg ctg agg agt<br>Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg Ser<br>260 265 270     | 1412 |
| ttc ctg aag gct ggc gga gaa gtg atc gac tct ctt aca tgg cat cac<br>Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His His<br>275 280 285     | 1460 |
| tat tac ttg aat gga cgc atc gct acc aaa gaa gat ttt ctg agc tct<br>Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser Ser<br>290 295 300 305 | 1508 |
| gat gcg ctg gac act ttt att ctc tct gtg caa aaa att ctg aag gtc<br>Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys Val<br>310 315 320     | 1556 |
| act aaa gag atc aca cct ggc aag aag gtc tgg ttg gga gag acg agc<br>Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser<br>325 330 335     | 1604 |
| tca gct tac ggt ggc ggt gca ccc ttg ctg tcc aac acc ttt gca gct<br>Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala Ala<br>340 345 350     | 1652 |
| ggc ttt atg tgg ctg gat aaa ttg ggc ctg tca gcc cag atg ggc ata<br>Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly Ile<br>355 360 365     | 1700 |
| gaa gtc gtg atg agg cag gtg ttc ttc gga gca gcc aac tac cac tta<br>Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu<br>370 375 380 385 | 1748 |
| gtg gat gaa aac ttt gag cct tta cct gat tac tgg ctc tct ctt ctg<br>Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu<br>390 395 400     | 1796 |
| ttc aag aaa ctg gta ggt ccc agg gtg tta ctg tca aga gtg aaa ggc<br>Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys Gly<br>405 410 415     | 1844 |
| cca gac agg agc aaa ctc cga gtg tat ctc cac tgc act aac gtc tat<br>Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val Tyr<br>420 425 430     | 1892 |
| cac cca cga tat cag gaa gga gat cta act ctg tat gtc ctg aac ctc<br>His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn Leu<br>435 440 445     | 1940 |
| cat aat gtc acc aag cac ttg aag gta ccg cct ccg ttg ttc agg aaa<br>His Asn Val Thr Lys His Leu Lys Val Pro Pro Leu Phe Arg Lys<br>450 455 460 465     | 1988 |
| cca gtg gat acg tac ctt ctg aag cct tcc ggc ccg gat gga tta ctt<br>Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu Leu<br>470 475 480     | 2036 |
| tcc aaa tct gtc caa ctg aac ggt caa att ctg aag atg gtg gat gag<br>Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp Glu<br>485 490 495     | 2084 |
| cag acc ctg cca gct ttg aca gaa aaa cct ctc ccc gca gga agt gca<br>Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser Ala<br>500 505 510     | 2132 |
| cta agc ctg cct gcc ttt tcc tat ggt ttt ttt gtc ata aga aat gcc<br>Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn Ala<br>515 520 525     | 2180 |
| aaa atc gct gct tgt ata tgaaaataaa aggcatatcgg taccctgag  | 2228 |

Lys Ile Ala Ala Cys Ile  
530 535

acaaaagccg aggggggtgt tattcataaa acaaaaccct agtttaggag gccacctcct 2288  
tgccgagttc cagagcttcg ggaggggtgg gtacacttca gtattacatt cagtgtggtg 2348  
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<210> 46

<211> 385

<212> DNA

<213> Rattus norvegicus

<400> 46

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cggttcctca ccttcctgag ctctccacgg cttcgagccc tgtctagagg cttatctcct 240  
gcgtacttga gatttggcgg caccaagact gacttcctta tttttgatcc caacaacgaa 300  
cccacctctg aagaaagaag ttactggcaa tctcaagaca acaatgatat ttgcgggtct 360  
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<210> 47

<211> 541

<212> DNA

<213> Rattus norvegicus

<220>

<221> misc\_feature

<222> (507)..(507)

<223> Any nucleotide

<400> 47

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cattaactgt caccacctgc agtggctctac ttagagaaca ccgactgga tgttaacact 180  
gaagcgcgtg ccccgccctc ccgaggtctt ggatccagcg ttgaagcttg ccccgccctc 240  
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atttcttatg acaaaaaacc cataggaaaa ggcgggcacg cttagtgagc ttctgcggg 480  
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<210> 48

<211> 127

<212> PRT

<213> Rattus norvegicus

&lt;400&gt; 48

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 20 25 30

Phe Tyr Thr Lys Arg Leu Phe Gln Ser Val Ser Pro Ser Phe Leu Ser  
 35 40 45

Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu Thr Phe  
 50 55 60

Leu Ser Ser Pro Arg Leu Arg Ala Leu Ser Arg Gly Leu Ser Pro Ala  
 65 70 75 80

Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro  
 85 90 95

Asn Asn Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Gln Ser Gln Asp  
 100 105 110

Asn Asn Asp Ile Cys Gly Ser Asp Arg Val Ser Ala Asp Val Leu  
 115 120 125

&lt;210&gt; 49

&lt;211&gt; 44

&lt;212&gt; PRT

&lt;213&gt; Rattus norvegicus

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (9)..(9)

&lt;223&gt; Xaa can be any naturally occurring amino acid

&lt;400&gt; 49

Leu Lys Met Val Asp Glu Gln Thr Xaa Pro Ala Leu Thr Glu Lys Pro  
 1 5 10 15

Leu Pro Ala Gly Ser Ser Leu Ser Val Pro Ala Phe Ser Tyr Gly Phe  
 20 25 30

Phe Val Ile Arg Asn Ala Lys Ile Ala Ala Cys Ile  
 35 40